

# A Case Report of the Treatment of Diabetic Foot Ulcers Using a Sodium Hyaluronate and Iodine Complex

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*Diabetic foot ulcers are difficult to heal due to defects in local microvasculature and persistent, concomitant infection. Despite the best medical care, amputation is often a management option for this problem. The authors have developed a new and unique system for wound treatment, which is based on a combination of high molecular weight sodium hyaluronate with an iodine complex—Hyiodine® (Contipro C, Dolní Dobrouč, Czech Republic). In this case report, the authors present an observational study on a series of patients with diabetic foot disease with nonhealing wounds treated with Hyiodine. The effect of the HA-iodine complex was studied on 18 patients suffering from complicated foot diabetic*

*wounds. The HA-iodine complex was either spread directly over the wound, or more frequently, gauze was immersed in the HA-iodine complex and then put on/into the wound. Then several layers of dry gauze covered the wound. This dressing was changed every 24 hours. Wound healing was monitored daily, and wound pictures were taken each second week. Clinical improvement was observed in the majority. This suggests that the HA-iodine complex dressing has potential that needs to be developed from controlled studies.*

**Key words:** diabetic foot disease, ischemia, infection, wounds, hyaluronain

Pecoraro reported that some 90% of lower extremity amputations in developed countries are the result of nonhealing wounds in patients with diabetes mellitus.<sup>1</sup> Minor foot trauma together with neuropathy and foot deformity were associated with 63% of diabetic foot ulcers.<sup>2</sup> However, it should be stressed that in 69% to 80% of cases, minor trauma precedes amputation; such trauma is preventable.<sup>1</sup> Early diagnosis and treatment of the ulceration can play a crucial role in defect development.<sup>3</sup>

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The complex management of diabetic foot ulcers consists of both local and systemic treatments, off-loading for pressure relief, and treating the infection. Wound dressings play an important part; successful wound management may result in a substantial reduction in morbidity.<sup>4</sup> In this case report, the authors present observational studies using a new dressing using hyaluronic acid (HA). This is a nonsulfated glycosaminoglycan, which is an integral part of the extracellular matrix.

HA is a natural component of the extracellular matrix that creates a hydrophilic environment; controls water retention, ionic and molecular diffusion; forms 3-dimensional structures; and plays an important role in the process of tissue repair.<sup>4</sup> A unique characteristic of HA is its hydration capacity. Hydrated HA contains approximately 1000-fold more water than polymer saccharides. This creates a moisture environment suitable for the migration of cells to new tissue sites and offers

**Table 1.** Study Group

	Number of Patients	Male/Female
Age (mean $\pm$ SD)	67.9 $\pm$ 10.0 years	
Wound area (mean $\pm$ SD)	35.6 $\pm$ 41.9 cm <sup>2</sup>	
Wound classification		
Wagner I (superficial wound)	1 patient	1/0
Wagner II (deep wound)	7 patients	4/3
Wagner III (deep wound and bone involved)	8 patients	5/3
Wagner IV (gangrene)	2 patients	1/1

protection to cells and extracellular matrix molecules, which can have a beneficial effect on the healing of both acute and chronic wounds.<sup>5,6</sup>

We have developed a complex of high molecular hyaluronate with iodine. We have previously reported on the usefulness of this approach in the bandaging of infected and difficult-to-treat wounds.<sup>7</sup> We reported the use of this treatment in patients with diabetic foot problems in a series of observational studies.

#### PATIENTS AND STUDY DESIGN

The study was performed at the diabetology division of the Department of Metabolic Care and Gerontology, Hradec Kralove Medical Faculty. The effect of the hyaluronan-iodine complex was studied in 18 patients suffering from complicated diabetic wounds localized in the lower extremities. The diabetic wounds were classified mostly as degrees II and III according to the Wagner scale. Only 1 patient was classified as Wagner I and 1 as Wagner IV—gangrene of the big toe (see Table 1). All patients suffered from peripheral neuropathy. A diagnosis of peripheral ischemia was made when there were unpalpable pulses on the dorsal foot artery and tibial posterior artery. Clinical assessment was confirmed by Doppler ultrasound measurement of ABPI in 8 patients.

None of these patients was suitable for intra-arterial angioplasty or surgical revascularization. All but 1 patient who was included in the study were referred for amputation. All patients agreed to participate in our study using this novel treatment. Patients were treated as in-patients until there was substantial or complete wound healing. All patients had at least 30 weeks' follow-up from the initiation of treatment. All patients were on bed rest during the hospital stay. During the home treatment, they were advised to offload the pressure and not to walk. Special orthopedic shoes were advised and prepared for patients.

Wound healing was monitored daily, and wound pictures were taken with a digital camera (Camedia, Olympus, Center Valley, Pa) to document the wound-healing process every other week. We documented the effect of the hyaluronan-iodine complex treatment and the time taken to achieve healing.

There were no patients with the Charcot foot. Full details of the patients and wounds are presented in Table 2.

#### Wound Dressing

The hyaluronan-iodine complex (Hyiodine®, Contipro C, Dolní Dobrouč, Czech Republic) is a viscous 1.5% solution of high molecular weight (1.5 MDa) sodium hyaluronan and 0.1% iodine. A sterile cotton gauze was immersed in this solution, and then the entire wound surface was covered with this soaked gauze. In the cases of deep wounds, the complex was directly squirted into the wound using a syringe. Then the defect was subsequently filled with gauze soaked in Hyiodine. The immersed gauze layers on the wound surface were then covered with several layers of sterile dry gauze. The wound dressing was changed each day.

When the wound condition improved, the patient was discharged from the hospital. At home, the hyaluronan-iodine wound dressings were placed on the respective wound by a specialized nurse or by a general practitioner every day or every other day. The patients were checked in our outpatient clinic at fortnightly intervals until wound healing was complete.

#### RESULTS

The data are presented in tabular form in Table 2. Complete healing was evident in 12 patients within 6 to 20 weeks of the start of treatment, depending on the wound's nature, localization, and extent. One wound in the diabetic foot have not healed yet. Wound treatment was unsuccessful in 2 patients who had ischemic defects; however, these patients were not suitable for reconstructive angioplasty or surgery.

It is apparent from the data presented in Table 2 that treatment of lower extremity diabetic wounds using the hyaluronan-iodine complex was effective in the majority of the diabetic patients. No side effects or allergic reactions were apparent during local treatment. Some patients felt pain at the place of the wound over the first few days after complex application. All amputations were made among patients with incurable arterial stenoses or with ongoing gangrenes of fingers or big

**Table 2.** Individual Patients and Effect of Hyaluronate-Iodine Complex Treatment

No.	Sex	Age	DM Type	Localization of Defect	Width (cm)	Length (cm)	Depth (cm)	Grade Wagner	Peripheral Arterial Disease	Time to Granulation (days)	Time to Complete Healing (days)	Amputation Localization
1	M	56	2	Plantar area	4	12	2	2	No	49	98	
2	M	75	2	Heel	2	3	2	3	Yes	79	145	
3	M	48	1	Plantar area	3	15	3	3	No	72	129	
4	M	71	1	Between toes	1	1	3	2	Yes	22	52	
5	F	72	2	Between toes	2	2	1	2	Yes	21	72	
6	M	63	2	Heel	3	5	4	3	No	63	130	
7	F	54	1	Calf <sup>a</sup>	4	12	0.5	1	No	19	45	
8	M	52	1	Big toe	2	1	3	2	No	35	52	
9	F	52	1	Heel	3	8	2	2	No	99	340	
10	M	55	1	Big toe	2	3	2	3	No	28	115	
11	M	62	1	Arch	2	11	1	2	No	6	18	
12	F	74	2	Big toe, medial foot	6	10	1	3	Yes	40	Amputation	Calf
13	M	65	1	Heel	9	12	0.5	2	Yes	32	488	
14	F	50	1	Plantar area	5	9	3	3	No	65	198	
15	M	52	1	Big toe	1	1	1	3	No	16	43	
16	F	58	2	Plantar area	3	9	2	4	Yes	53	86	Big toe
17	M	78	2	Instep toes	12	14	2	4	Yes	63	<sup>b</sup>	Two toes
18	M	77	2	Big toe, plantar area	5	2	1	4	Yes	14	Amputation	Calf
Mean		61.9			3.8	7.2	1.9	2,7		43.1	133.4	
SD		10.0			2.8	4.8	1.0	0.8		25.3	122.1	

a. Nonhealing defect after venous graft removal due to aorto-coronary bypass.

b. The wound had not healed completely; however, significant improvement was apparent.



Fig 1. Patient 1. Deep wound between the fourth and fifth toes on the right leg before the treatment.



Fig 2. Patient 1. Twenty days after the onset of the hyaluronan-iodine complex treatment, the wound is filled with granulation tissue.

toes. Small surgical procedures had to be completed in patients with pus retention and signs of continual inflammation. The effect of this treatment may be viewed in the attached photographic figures.

## DISCUSSION

This is a report of uncontrolled observations using a dressing system that we have devised and



Fig 3. Patient 1. Complete wound healing after 2 months of the treatment.



Fig 4. Patient 2. Plantar is after large surgical debridement, before the hyaluronan-iodine complex treatment.



Fig 5. Patient 2. Two months after the onset of treatment, the wound was filled with granulation tissue.



Fig 6. Patient 2. Complete wound healing after 5 months of the hyaluronan-iodine complex treatment.



Fig 7. Patient 3. Large and deep plantar wound approaching the heel bone.



Fig 8. Patient 3. Wound filled with granulation tissue after 49 days of the hyaluronan-iodine complex treatment.

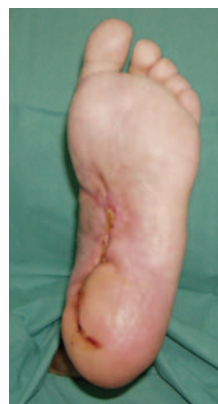


Fig 9. Patient 3. Complete wound healing after 88 days of treatment.

**Table 3.** Effect of Diabetic Wound Treatment Using Hyaluronate-Iodine Complex Treatment

Treatment Outcome	Number of Patients
Complete healing	14
Still treated	1
Amputations	4 <sup>a</sup>
Length of Treatment	(mean ± SD)
Wound filled with granulation tissue	43.6 ± 25.0 days
Complete healing	133.8 ± 122.1 days

a. In all cases of amputation, patients had untreatable vascular occlusions. In 3 patients with subsequent amputation, tissue necroses and gangrene were present at the start of treatment.

used on patients with difficult-to-heal diabetic foot ulcers. We are aware of the limitations of this study. We realize that the findings presented in this report are classified a low level of evidence; nonetheless, given the difficult clinical problem, this report must be considered in perspective.

This new dressing system<sup>7</sup> is based on a combination of high molecular sodium hyaluronan and iodine, and we reported its healing efficacy in wounds of different etiologies.<sup>7,8</sup> In this present observational study, we have observed diabetic foot wounds responding to this wound-dressing complex. The patients we treated had difficult-to-heal wounds, as may be observed from Tables 2 and 3 where the data presented include the number of patients who underwent subsequent amputations. To the best of our knowledge, this is the first report of the use of a hyaluronan-iodine-iodide complex for wound treatment.

It would be speculative to discuss how this wound complex works; before doing so, we would expect to see data from controlled clinical observations. All we would wish to observe is that the wound complex appears to be a versatile agent.<sup>9</sup>

### Does Hyaluronan Work as a Wound Treatment?

The results are encouraging but not conclusive; some are positive<sup>10</sup> and others less so.<sup>11</sup> Our study was an observational one on patients with

difficult-to-heal diabetic foot wounds. The results using this wound complex are encouraging and beg further controlled randomized studies to elicit its full value in treating a difficult problem.

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